

wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and

(c) a polypeptide having activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence and fails to support packaging of the helper adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

3. (Amended) The vector system of claim 2, wherein the helper-dependent and helper adenovirus serotypes are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40).

4. (Amended) The vector system of claim 2, wherein the helper-dependent adenovirus serotype is adenovirus type 5 and the helper adenovirus serotype is adenovirus type 7.

5. (Amended) The vector system of claim 2, wherein the helper-dependent adenovirus serotype is adenovirus type 7 and the helper adenovirus serotype is adenovirus type 5.

6. (Amended) The vector system of claim 1, wherein the helper-dependent adenovirus sequence fails to produce a complete adenovirus capsid.

7. (Amended) The vector system of claim 6, wherein the helper-dependent adenovirus sequence is encapsidated in a capsid comprising at least one polypeptide encoded by the helper adenovirus sequence.

8. (Amended) The vector system of claim 6, wherein the helper-dependent adenovirus sequence is packaged in a capsid encoded by the helper adenovirus sequence.

B²
9. (Amended) The vector system of claim 42, wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene or hexon gene or combination thereof.

10. (Amended) The vector system of claim 1, wherein the failure to produce a functional 52/55 kDa trans-acting protein is due to a mutation in the sequence encoding the protein.

12. (Amended) The vector system of claim 1, wherein the helper adenovirus sequence further comprises a nucleic acid sequence encoding the polypeptide having the activity of the 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid.

BB
SUB
D²
13. (Amended) The vector system of claim 1, wherein the polypeptide having the activity of the 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence is encoded by a nucleic acid sequence functionally-associated with the genome of an adenovirus replication competent host cell.

15. (Amended) The vector system of claim 1, wherein the polypeptide having the activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence is a 52/55 kDa trans-acting protein.

B⁴
16. (Amended) The vector system of claim 1, wherein the helper-dependent adenovirus sequence lacks at least one nucleic acid sequence needed to produce a capsid and further comprises a nucleic acid sequence encoding a polypeptide having the activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence.

SUB
D³
17. (Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the vector system comprising:

- (a) a helper-dependent adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;

- 54B 3
①
- (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a heterologous nucleic acid;
 - (b) a helper adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a nucleic acid sequence encoding a polypeptide having the activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence and fails to support packaging of the helper adenovirus nucleic acid sequence,
- wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

B⁴

18. (Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the vector system comprising:

- (a) a helper-dependent adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a heterologous nucleic acid;
 - b) a helper adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence,
- wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and
- (c) a cell comprising a nucleic acid sequence encoding a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein,
- wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

19. (Amended) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the vector system comprising:

- 5613 4
①
- B⁴
- (a) a helper-dependent adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a heterologous nucleic acid;
 - (b) a helper adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence,wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and
 - (c) an expression cassette comprising a nucleic acid sequence encoding a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein, wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

20. (Amended) A vector comprising a replication defective adenovirus sequence comprising:

- (a) a helper-dependent adenovirus serotype-specific cis-acting packaging sequence;
 - (b) a nucleic acid sequence encoding a functional helper adenovirus serotype-specific 52/55 kDa trans-acting protein, wherein the helper adenovirus serotype 52/55 kDa trans-acting protein does not have the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein, lacking the ability to produce a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein,
- wherein the replication defective adenovirus sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

B⁵

23. (Amended) The vector of claim 20, wherein the helper-dependent and helper adenovirus serotypes are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5

(Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40).

24. (Amended) The vector of claim 23, wherein the helper-dependent adenovirus serotype is adenovirus type 5 and the helper adenovirus serotype is adenovirus type 7.

25 (Amended) The vector of claim 23, wherein the helper-dependent adenovirus serotype is adenovirus type 7 and the helper adenovirus serotype is adenovirus type 5.

27. (Amended) A kit for making adenovirus encapsidated replication defective nucleic acid sequences comprising:

(a) a helper-dependent adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
- (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a heterologous nucleic acid;

(b) a helper adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus ITRs;
- (ii) an adenovirus serotype-specific cis-acting packaging sequence, wherein the

helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and

(c) a nucleic acid sequence encoding a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

28. (Amended) The kit of claim 27, wherein the polypeptide having the activity of the 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence is encoded by a nucleic acid sequence functionally-associated with the genome of an adenovirus replication competent host cell.

29. (Amended) The kit of claim 27, wherein the nucleic acid sequence encoding a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein further comprises an expression cassette.

30. (Amended) The kit of claim 27, wherein the helper adenovirus sequence further comprises the nucleic acid sequence encoding a polypeptide having the activity of a helper-dependent adenovirus serotype 52/55 kDa trans-acting protein.

31. (Amended) A method of producing a replication defective encapsidated adenovirus gene transfer vector, comprising the following steps:

(a) transforming or infecting into adenovirus replication competent host cells

(i) a helper-dependent adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus inverted terminal repeats (ITRs);

an adenovirus serotype-specific cis-acting packaging sequence; and

a heterologous gene;

(ii) a helper adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus ITRs;

an adenovirus serotype-specific cis-acting packaging sequence,

wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and

(iii) a nucleic acid sequence encoding a polypeptide having the activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence and fails to support packaging of the helper adenovirus nucleic acid sequence; and

(b) culturing the cells under conditions where the helper-dependent replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus gene transfer vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

32. (Amended) A method of producing a replication defective encapsidated adenovirus gene transfer vector, comprising the following steps:

(a) transforming or infecting into an adenovirus replication competent host cell two adenovirus replication defective sequences, wherein the cell comprises a nucleic acid sequence encoding a polypeptide having the activity of an adenovirus serotype 52/55 kDa trans-acting protein that supports packaging of a helper-dependent adenovirus nucleic acid sequence and fails to support packaging of a helper adenovirus nucleic acid sequence,

(i) a helper-dependent adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus inverted terminal repeats (ITRs);
an adenovirus serotype-specific cis-acting packaging sequence; and
a heterologous gene;

(ii) a helper adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus ITRs;
an adenovirus serotype-specific cis-acting packaging sequence,

wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and

(b) culturing the cells under conditions where the helper-dependent replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus gene transfer vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

33. (Amended) A method of producing a replication defective encapsidated adenovirus gene transfer vector, comprising the following steps:

(a) transforming or infecting two adenovirus replication defective sequences into an adenovirus replication competent host cell, wherein the two sequences comprise:

(i) a helper-dependent adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus inverted terminal repeats (ITRs);

Handwritten notes: "SUB D" with a circled "D" and a checkmark.

an adenovirus serotype-specific cis-acting packaging sequence;
a heterologous gene; and
a nucleic acid sequence encoding a polypeptide having the activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence and fails to support packaging of the helper adenovirus nucleic acid sequence; and

(ii) a helper adenovirus nucleic acid sequence comprising:

5' and 3' adenovirus ITRs;
an adenovirus serotype-specific cis-acting packaging sequence,
wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and

(b) culturing the cells under conditions where the helper-dependent replication defective adenovirus sequence is encapsidated to produce a replication defective adenovirus gene transfer vector,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

34. (Amended) The method of claim 31, 32, or 33 wherein the helper adenovirus sequence further comprises an adenoviral nucleic acid sequence encoding a complete adenoviral viral capsid.

35. (Amended) A vector for selectively packaging replication defective nucleic acid sequences in adenovirus capsids, the vector comprising:

- (a) a replication defective adenovirus sequence comprising an adenovirus serotype 7 (Ad7) cis-acting packaging sequence;
- (b) a nucleic acid sequence encoding a polypeptide having the activity of an adenovirus serotype 5 (Ad5) 52/55 kDa trans-acting protein; and
- (c) an adenoviral nucleic acid sequence [to] that encodes a viral capsid and fails to encode or produce a polypeptide having the activity of an adenovirus 7 serotype 52/55 kDa trans-acting protein.--

Please add claims 40-42.

--40. A packaging cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

- (a) a helper-dependent adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a heterologous nucleic acid;
- (b) a helper adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence,wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of the helper adenovirus serotype 52/55 kDa trans-acting protein; and
- (c) a polypeptide having activity of a 52/55 kDa trans-acting protein that supports packaging of the helper-dependent adenovirus nucleic acid sequence and fails to support packaging of the helper adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

41. A packaging cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

- (a) a nucleic acid sequence encoding a polypeptide having the activity of an adenovirus serotype-specific 52/55 kDa trans-acting protein;
- (b) a helper-dependent adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
 - (ii) an adenovirus serotype-specific cis-acting packaging sequence; and
 - (iii) a heterologous nucleic acid;
- (c) a helper adenovirus nucleic acid sequence comprising:
 - (i) 5' and 3' adenovirus ITRs;

B
SUB
D⁷

(ii) an adenovirus serotype-specific cis-acting packaging sequence that fails to support the activity of the polypeptide having the activity of an adenovirus serotype-specific 52/55 kDa trans-acting protein,

wherein the replication defective adenovirus comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, a penton gene, a fiber gene or a hexon gene, or a combination thereof.

42. A vector system for selectively packaging a replication defective nucleic acid sequence in a virus capsid, the vector system comprising:

(a) a helper-dependent adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' viral inverted terminal repeats (ITRs);
- (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a heterologous nucleic acid,

wherein the helper-dependent adenovirus nucleic acid fails to produce a polypeptide having the activity of a serotype-specific 52/55 kDa trans-acting protein specific for the first adenovirus serotype-specific cis-acting packaging sequence;

(b) a helper adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' virus ITRs;
- (ii) a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the helper adenovirus nucleic acid fails to produce a polypeptide having the activity of a serotype-specific 52/55 kDa trans-acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(c) a nucleic acid encoding a polypeptide or a polypeptide having an activity of a serotype-specific 52/55 kDa trans-acting protein that supports packaging of the first adenovirus serotype-specific cis-acting packaging sequence and fails to support packaging of the second adenovirus serotype-specific cis-acting packaging sequence.--

B
SUB
D